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(54) Title: MARKER GENE

(57) Abstract: A method of determining a predisposition to infection, especially infection with HIV, together with therapy for the infection is described.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/04493

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 C12Q1/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, MEDLINE, EPO-Internal, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KRUMLAUF R. ET AL.: "CONSTRUCTION AND CHARACTERIZATION OF GENOMIC LIBRARIES FROM SPECIFIC HUMAN CHROMOSOMES" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 79, no. 9, 1982, pages 2971-2975, XP002276750 ISSN: 0027-8424 paragraph bridging pages 2971-2972 --- -/--	16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *8* document member of the same patent family

Date of the actual completion of the international search

27 April 2004

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INTERNATIONAL SEARCH REPORT

II International Application No

P 03/04493

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DUNHAM I. ET AL.: "THE DNA SEQUENCE OF HUMAN CHROMOSOME 22" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 402, no. 6761, 2 December 1999 (1999-12-02), pages 489-495, XP001180206 ISSN: 0028-0836 the whole document	16,61-65
A	WO 00/61811 A (SMITH M.W. ET AL.) 19 October 2000 (2000-10-19) abstract; claims 1-27	1-21, 38-46, 51,57, 61-67
A	HOGAN C.M. ET AL.: "Host determinants in HIV infection and disease: Part 2: Genetic factors and implications for antiretroviral therapeutics" ANNALS OF INTERNAL MEDICINE, vol. 134, no. 10, 15 May 2001 (2001-05-15), pages 978-996, XP002276751 ISSN: 0003-4819 the whole document	1-21, 38-46, 51,57, 61-67
A	O'BRIEN S.J. ET AL.: "Polygenic and multifactorial disease gene association in man: Lessons from AIDS." ANNUAL REVIEW OF GENETICS. UNITED STATES 2000, vol. 34, 2000, pages 563-591, XP002276752 ISSN: 0066-4197 abstract; table 2 page 582, line 5-14	1-21, 38-46, 51,57, 61-67
A	DEAN M. ET AL.: "GENETIC RESTRICTION OF HIV-1 INFECTION AND PROGRESSION TO AIDS BY A DELETION ALLELE OF THE CKR5 STRUCTURAL GENE" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 273, 27 September 1996 (1996-09-27), pages 1856-1862, XP000198489 ISSN: 0036-8075 abstract; figures 2,3	1-21, 38-46, 51,57, 61-67

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 03/04493

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ROWLAND-JONES S.L. ET AL.: "Immune response in HIV-exposed seronegatives: Have they repelled the virus?" CURRENT OPINION IN IMMUNOLOGY, vol. 7, no. 4, 1995, pages 448-455, XP001180618 ISSN: 0952-7915 cited in the application the whole document</p> <p>---</p>	1-21, 38-46, 51,57, 61-67
A	<p>SHEARER G.M. ET AL.: "Protective immunity against HIV infection: has nature done the experiment for us?" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 17, no. 1, 1996, pages 21-24, XP004034638 ISSN: 0167-5699 cited in the application the whole document</p> <p>---</p>	1-21, 38-46, 51,57, 61-67
A	<p>HASENKRUG K.J. ET AL.: "Immunity to retroviral infection: the Friend virus model." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. UNITED STATES 22 JUL 1997, vol. 94, no. 15, 22 July 1997 (1997-07-22), pages 7811-7816, XP002276754 ISSN: 0027-8424 the whole document</p> <p>---</p>	1-21, 38-46, 51,57, 61-67
A	<p>GHOSH S. ET AL.: "The Finland-United States investigation of non-insulin-dependent diabetes mellitus genetics (FUSION) study. I. An autosomal genome scan for genes that predispose to type 2 diabetes" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 67, no. 5, November 2000 (2000-11), pages 1174-1185, XP002276755 ISSN: 0002-9297 abstract</p> <p>---</p>	16,61-65
A	<p>TOREN AMOS ET AL: "Genetic linkage of autosomal-dominant Alport syndrome with leukocyte inclusions and macrothrombocytopenia (Fechtner syndrome) to chromosome 22q11-13" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 65, no. 6, December 1999 (1999-12), pages 1711-1717, XP002276756 ISSN: 0002-9297 abstract</p> <p>-----</p>	16,61-65

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/04493

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 1-7 and 9-13 are directed to a diagnostic method encompassing a potential surgical step ("obtaining a DNA bearing sample from a subject"), the search has been carried out for the corresponding methods lacking said surgical step.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 14-15, 49, 57, 61-63, and 66-67 (all partially), 22-37, 47-48, 50, 52-56, 58-60, 68-70 (completely)

Claims 14-15 relate to kits which are suitable for the diagnosis of a predisposition to infection and which comprise reagents for determination of genotype of at least one of a group of microsatellite loci. Since, however, said reagents are not defined in terms of technical features (e.g. the sequences of PCR primers), the skilled person is not able to determine which reagents fall under the wording of said claims. Consequently, lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for kits comprising those reagents which are disclosed in the present application as being suitable for determining the genotype of at least one of the listed microsatellite loci, i.e. primers having the sequences shown in SEQ ID NO's 1-10.

Claims 22-37 and 47-50 relate to compositions, contraceptives, chips or assay plates, or uses thereof, comprising a polypeptide "encoded by the gene located in the chromosomal segment adjacent to" a defined group of microsatellite loci. Since, however, neither said "gene" itself nor the "chromosomal segment adjacent to" said loci is clearly and unambiguously defined in the present application, the skilled person is totally unable to understand which gene product is meant in claims 22-37. Consequently, said claims cannot be searched.

Claim 52 relates to an immunoglobulin A defined by a desirable property ("providing resistance to infection") and by reference to the procedure of its production ("produced according to claim 50 or 51"). Since, however, said claim does not contain any technical features defining said immunoglobulin A, the skilled person is not in the position to clearly and unambiguously the nature of said immunoglobulin A. Thus, in the absence of any technical features of said immunoglobulin A, a meaningful search is impossible for claim 52. Consequently, claims 53-56 and 58-60 cannot be searched either, because they refer back to claim 52.

Claims 61-63 relate to a nucleic acid defined only in terms the function of its product ("controlling the production of neutralizing antibodies to HIV"). Since, however, said claims provide no technical features of the nucleic acid locus (chromosomal position, sequence?), the skilled person is totally unable to understand which nucleic acids fall under the wording of said claims. Therefore, lack of clarity (Article 6 PCT) arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of claims 61-63 which do appear to be clear, namely the subject-matter of claims 64-65.

Claims 49, 57, and 66-67 have only been searched partially, i.e. the search has been restricted to those parts of said claims which depend on searched claims. In other words, claim 49 has only been search as far as it depends on claims 45-46, claim 57 only as far as it depends on claim

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

51, and claims 66-67 as far as they depend on claims 64-65.

Finally, a meaningful search is also impossible for claims 68-70, because they relate to gene products (or medical use thereof) which are only defined in terms of the genomic loci encoding them. Since, however, said loci are very large, the skilled person is not able to determine which gene products are meant. Consequently, a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of said claims impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

tional Application No

03/04493

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0061811	A	19-10-2000	AU WO	4334400 A 0061811 A2	14-11-2000 19-10-2000